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Original Contribution

Characteristics and outcomes of in-hospital cardiac arrest in adults hospitalized with acute coronary syndrome in China☆

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ABSTRACT

Aims: This retrospective study aims to analyze and explore the clinical characteristics, risk factors, and in-hospital outcomes - including return of spontaneous circulation (ROSC) and survival to discharge - of hospitalized patients admitted with acute coronary syndrome (ACS) suffering cardiac arrest.
Methods: ACS patients admitted to three tertiary hospitals in Fujian, China, were evaluated retrospectively from January 1, 2012 to December 30, 2016. Data were collected, based on the Utstein Style, for all cases of attempted resuscitation for IHCA. We analyzed patient characteristics, pre-event variables, event variables, and the main outcomes, including ROSC and survival to discharge, and identified the influencing factors on the outcomes.
Results: The total number of ACS admissions across the three hospitals during this study period was 21,337. Among these admissions, 320 ACS patients experienced IHCA (incidence: 1.50%); 134 (41.9%) patients experienced ROSC; and 68 (21.2%) survived to discharge. The findings indicated that four factors were associated with ROSC, including age <70 years-old, shockable rhythm, duration of resuscitation (≤15 min and 16–30 min), and PCI. Five factors were associated with survival to discharge, including age <70 years-old, shockable rhythm, the duration of resuscitation (≤15 min and 16–30 min), Killip ≤ II, and CCI ≤ 2.
Conclusion: Younger age, shockable rhythm, and shorter duration of resuscitation were all factors demonstrated to be a predictor of ROSC and survival to hospital discharge.

1. Introduction

The most common cause of in-hospital cardiac arrest (IHCA) is usually myocardial ischemia or infarction [1], with nearly 50% due to cardiovascular disease [2]. Cardiac arrest is a fatal complication of acute coronary syndrome (ACS) during hospitalization. Patients suffering from ACS have approximately 1.4 million hospital admissions per year in the United States [3], and an annual incidence of approximately 6 events per 1000 admissions [4]. ACS has three different diagnoses, including acute ST-elevation myocardial infarction (STEMI), non-STEMI (NSTEMI) and unstable angina (UA) [5]. Previous studies have focused on highly selected myocardial infarction (MI) patients undergoing PCI or coronary artery bypass graft surgery (CABG), including STEMI [1,6,7] and NSTEMI [8,9], with the majority of the published studies conducted on patients suffering sudden death [10,11] or out-of-hospital cardiac arrest [12,13]. Few studies have been performed to investigate resuscitation outcomes after IHCA, based on an unselected cohort.

Several factors were associated with the resuscitation outcomes, such as ROSC and survival to discharge, including age [14-16], race [17], gender [18,19], comorbidity [20], smoking status [21,22], initial rhythm [23], and duration of resuscitation [24]. However, the impact of resuscitation outcomes on ACS patients is unclear.

While the epidemiology of IHCA has been extensively studied in both the United States and Europe [1,25,26], the incidences, demographics, comorbidities, disease patterns and outcomes of ACS patients in Asia have been believed to be different from those of patients in Western countries [27-29] due to wide variations between countries

☆ Characteristics and Outcomes of In-hospital Cardiac Arrest in Acute Coronary Syndrome in China.

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Abbreviations

ACS	acute coronary syndrome
CA	cardiac arrest
CCI	Charlson Comorbidity Index
IHCA	in-hospital cardiac arrest
NSTEMI	acute non-ST segment elevation myocardial infarction
PEA	pulseless electrical activity
PVT	pulseless ventricular tachycardia
ROSC	return of spontaneous circulation
STEMI	acute ST-segment elevation myocardial infarction
UA	unstable angina
VF	ventricular fibrillation

in terms of ethnicity, geographical location, social and healthcare systems, medications, and invasive cardiac procedures. In China, there is a paucity of IHCA data on patients admitted with ACS. Some Chinese studies have focused on hospitalized patients overall, and not only on patients with ACS [2,30]. In one study, participants even included patients who had suffered a cardiac arrest in hospital or outside of the hospital [30]. Some studies that examined in-hospital outcomes among cardiac arrest patients have been single-center studies [30]. Therefore, we conducted this investigation on ACS patients to describe the characteristics of patients with IHCA, to determine the independent predictors for resuscitation outcomes after IHCA.

2. Methods

2.1. Study design and setting

We performed a retrospective cohort review at three tertiary hospitals in Fujian province, China, on ACS patients who were discharged from January 2012 to December 2016. The participant hospitals, including two comprehensive hospitals and one specialist hospital, respectively saw approximately 1200, 2500 and 1900 ACS patient admissions annually. All physicians and nurses are required to receive Advanced Cardiac Life Support training, to ensure their ability to resuscitate patients.

2.2. Study populations

At the participating hospitals, we identified a total of 21,337 ACS patients aged 18 years or older, who had undergone a resuscitation attempt (chest compression and/or defibrillation) complicated by cardiac arrest, from January 2012 to December 2016. Unstable angina (UA), acute ST-segment elevation myocardial infarction (STEMI) and acute non ST-segment elevation myocardial infarction (NSTEMI) were included. IHCA was defined by unresponsiveness, apnea, and the absence of a central palpable pulse due to pulseless ventricular tachycardia (PVT) or ventricular fibrillation (VF), pulseless electrical activity (PEA), bradycardia, or asystole. The exclusion criteria were: patients with cardiac arrest, whose family caregivers refused to have them resuscitated; those with missing data; as well as patients with prior out-of-hospital cardiac arrest and who were transported to hospital with ongoing resuscitation. For patients with more than one IHCA within the same hospitalization, only the first arrest was included.

2.3. Data collection

Our study group, which consisted of one cardiologist, one anesthetist, one nurse, one nursing master's student, one epidemiology master's student, and two nursing interns, collected data from April 2015 to January 2017. Our information was retrieved from patients' electronic medical records. The number of IHCAs was presented as the incidence per 1000 admissions.

The IHCA report sheet was designed based on the Utstein Style template [31]. It contained patient characteristics, pre-event variables, and event variables. **Patient characteristics covered** date of admission, age, gender, height, weight, drinking and smoking history, length of hospital stay before the event, and others. **Pre-event variables** included diagnosis of ACS, culprit artery, Killip classification, pre-existing Charlson Comorbidity Index (CCI), cardiac shock, monitoring, and others. CCI is a summed score assigning the severity-weighted points for chronic health conditions, which contains 17 chronic diseases, and can be used to assess the effect of total burden of disease [32]. **Event variables involved** location (intensive care unit, general ward, catheterization room, or others), initial rhythm (PVT and VF, PEA and asystole), resuscitation attempted, duration of resuscitation, and others.

2.4. Outcomes

The primary outcome of this study was survival to hospital discharge, and the secondary outcome was the immediate ROSC post-resuscitation. In this study, only ROSC of >20 min was considered to be sustained ROSC. Initiation of assisted circulation (e.g., extracorporeal membrane oxygenation) was not considered to be ROSC [33]. Death was defined as patients who did not respond to resuscitative efforts, or any ROSC patients who died in hospital or who were discharged in critical condition.

2.5. Statistical analysis

Descriptive statistics were reported as mean ± standard deviation, or median [interquartile range (IQR)] for continuous variables. For categorical variables, the percentages of patients in each category were calculated. Comparisons between categorical data were done by Chi-square test, and comparisons between continuous variables were done by Student's *t*-test. We used multivariate logistic regression models to identify factors that predicted ROSC and survival to discharge. Variables included age, gender, being a smoker, in-hospital location, length of stay before the event, Killip, pre-existing CCI, initial rhythm, duration of resuscitation, resuscitation attempt, and prior PCI. Using the enter method, selected variables were introduced to the logistic regression model on the basis of the Akaike information criterion. Interactions between the variables were tested using the Wald test. Results were reported using odds ratios (OR) and 95% confidence intervals (95% CI). Statistical analyses were carried out using SPSS software, version 22.0 (Chicago IL, USA). All significance tests used a 2-sided *p*-value <0.05.

3. Results

3.1. Patient characteristics

Among the 21,337 ACS patient admissions combined within the four-year study period, 412 ACS patients had an occurrence of IHCA in the participating hospitals. We excluded 44 cases where family caregivers had refused resuscitation before the event, and 48 cases where patients had suffered an out-of-hospital cardiac arrest before admission (Fig. 1). Our final population was composed of 320 in-hospital cardiac arrest ACS patients at three hospitals. The total IHCA incidence was 15.0 events per 1000 hospital admissions. The reported patients had an average age of 70.53 ± 11.82 years. Nearly half of the patients, 138 (43.1%), were younger than 70 years old; 231 (72.2%) were male, and 113 (35.3%) were smokers.

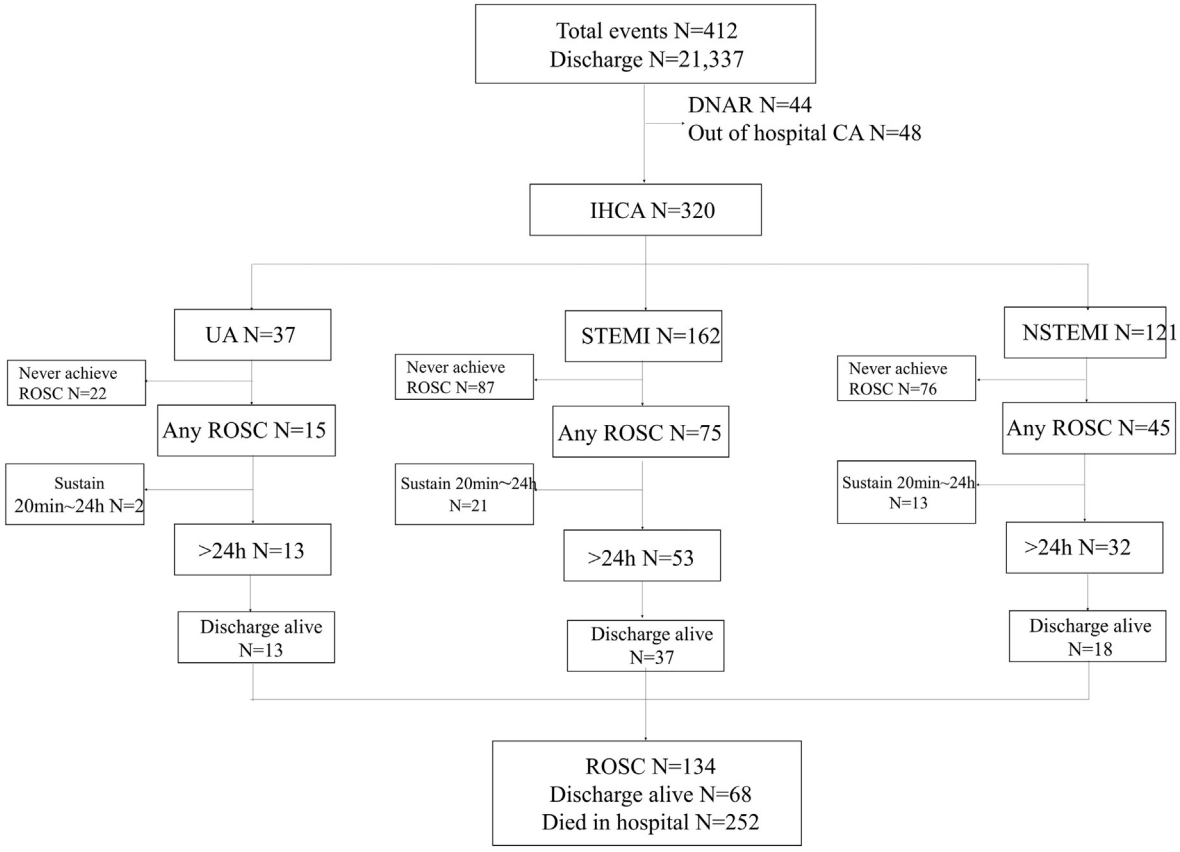

Fig. 1. Flow-chart of patient inclusion and outcomes.

3.2. Pre-event variables

The types of ACS were UA in 37 (11.6%) patients, STEMI in 162 (50.6%) patients, and NSTEMI in 121 (37.8%) patients. Sixty (18.8%) patients had one-vessel disease, 55 (17.2%) patients had two-vessel disease, and 112 (35.0%) patients had three-vessel disease; 31 (19.7%) patients had left main coronary artery disease complicated by multivessel disease, while 62 (19.4%) patients did not have a coronary angiography. The Killip classifications before events were I (45 cases), II (53 cases), III (162 cases), and IV (158 cases). The medium of CCI point was 2 (1–4). Ninety patients (28.1%) had PCI prior to the event (Table 1).

3.3. Event variables

A total of 295 (92.2%) cardiac arrests occurred in monitored patients. Nearly half of patients (140, 43.8%) had an initial cardiac rhythm that was shockable. The median duration of resuscitation was 32.50 (10.75–55.25) min. Of the 320 patients, more than one-half (194, 60.6%) were located in the ICU at the time of the IHCA; 87 (27.2%) patients had an event that initiated in the general ward, 33 (10.3%) arrests occurred in the catheterization room, and 6 (1.9%) arrests were recorded in transit, in the examination room or others (Table 1).

3.4. In-hospital outcomes and risk factors

A sustained ROSC was achieved in 134 (41.9%) patients, 68 of whom (50.75%; 21.2% of the initial cohort) survived to hospital discharge (Fig. 1). Univariate regression analysis found improved ROSC in patients age <70 years-old, smokers, or with prior PCI. Resuscitation in the catheterization room achieved a better outcome when compared to those in the ICU or a general ward. Of the 140 patients with shockable rhythm (VT/VF), 62.1% achieved ROSC and 37.9% survived to discharge. In patients with an initial rhythm of non-shockable rhythm (PEA/asystole), 26.1% achieved ROSC and 8.3% survived to discharge (Table 1). Duration of resuscitation was also significantly shorter in patients who achieved ROSC and survived to hospital discharge, compared to patients who did not achieve ROSC and did not survive to discharge (Table 2).

Multivariate logistic regression analyses showed that factors independently associated with ROSC included age <70 years-old, VF/VT, sustained resuscitation of ≤30 min, prior PCI (OR 4.78[2.17–10.95], 4.40 [1.92–10.06], 32.05[10.95–93.83], 5.34[1.92–10.06, 2.40[1.08–5.35], respectively). Age <70 years-old, VF/VT, sustained resuscitation of ≤15 min or 16–30 min, Killip ≤II, and CCI ≤2 points were independently associated with a higher likelihood of survival to discharge (OR 4.10 [1.67–10.02], 7.19[2.67–19.37], 73.02[18.83–283.13], 6.01[1.36–26.61], 5.63[2.02–15.66], 6.71[2.29–19.68], respectively) (Tables 3–4).

4. Discussion

This is the first multicenter study documenting incidence of IHCA in ACS patients in China. We calculated the incidence according to data obtained from three hospitals in four consecutive years. The incidence of IHCA from ACS (15 per 1000 hospital admissions) is much higher, compared to hospitalized patients overall suffering from all different kinds of disease, reported by other countries (4.02 in the United States [34],1.6 in the United Kingdom [35], and 1.51 in Italy [36]). We also observed that 41.9% of patients achieved ROSC, and 21.3% of patients survived to discharge, which were much higher figures than in data published historically [34-36].

4.1. Impact of initial rhythm on IHCA outcomes

Our data demonstrated that survival from IHCA was more than seven-fold higher in patients with initial documented shockable rhythm

Table 1
Characteristics of IHCA patients.

Variables	N (%)
Characteristics	
Age, years	70.53 ± 11.82[a]
Male	231 (72.2)
Female	89 (27.8)
Smoking	113 (35.3)
Drinking	47 (14.7)
Culprit artery	
One-vessel	60 (18.8)
Two-vessel	55 (17.2)
Three-vessel	112 (35.0)
Left main coronary artery + multivessel	31 (9.7)
Non-coronary angiography	62 (19.4)
Spetrum of ACS	
UA	37 (11.6)
STEMI	162 (50.6)
NSTEMI	121 (37.8)
Comorbidities	
Killip	
I	45 (14.1)
II	53 (16.6)
III	64 (20.0)
IV	158 (49.4)
CCI	2 (1–4)[c]
Cardiac shock	87 (27.2)
Respiratory failure	29 (9.1)
Hyperlipidemia	61 (19.1)
Hypertension	192 (60.0)
Prior PCI	90 (28.1)
Advanced support	
Not	17 (5.3)
Monitoring	295 (92.2)
Mechanical ventilation	39 (12.2)
Cardiac pacemaker	16 (5.0)
Location	
ICU	194 (60.6)
General ward	87 (27.2)
Catheterization room	33 (10.3)
Others	6 (1.9)
Resuscitation attempt[b]	
A	84 (26.3)
B	112 (35.0)
C	66 (20.6)
D	58 (18.1)
Length of hospital stay prior to cardiac arrest, days	2 (1–7)[c]
Duration of resuscitation, min	32.50(10.75–55.25)

[a] Means ± standard deviation.
[b] A:CPR or defibrillation; B:CPR + defibrillation; C: CPR + endotracheal intubation; D: CPR + defibrillation + endotracheal intubation.
[c] Medium (IQR).

(VT/VF), compared to patients with non-shockable rhythm (PEA or asystole). This is in accordance with previous multicenter study [37]. However, we had a higher proportion of initial shockable rhythm in the present study than that seen in a previously reported large retrospective study (43.8% vs 24%), which included not only ACS patients, but also patients in hospital with any kind of disease. We also had a slight advantage in terms of live discharge (21.3% vs 17.6%) [37]. In the present investigation, 43.8% of IHCA patients were associated with an initial rhythm of VT/VF, and these patients contributed to 62.1% of ROSC and 37.9% of survival to discharge. Conversely, 56.3% of IHCA patients were associated with an initial rhythm of PEA or asystole, and these patients contributed to 26.1% of ROSC and 8.3% of survival to discharge. It may be due to the fact that shockable rhythm indicates a recent onset of cardiac arrest, cardiac etiology, and a rhythm that can be treated promptly and often successfully with defibrillation [38]. A total of 92.2% patients in this study were monitored during the cardiac arrest event which was much higher than 60.5% reported by Radeschi et al. [36], whose cardiac arrest mostly occurred in general ward, conversely, ours were in ICU. Smith et al. has showed that patients under monitored were more likely to have shockable rhythms and survival advantage than those in non-monitored areas [39]. In our cohort, 60.6% of the cardiac arrest events occurred in the ICU or CCU, and 10.3% occurred in the catheterization room; both locations had adequate staffing and equipment, which allowed real-time monitoring and immediate defibrillation.

4.2. Impact of age on IHCA outcomes

Advanced age was previously reported in association with poorer outcomes [14,16]. The results of this study showed that patients aged <70 years-old have a >4 times higher chance of ROSC and survival to discharge compared to patients older than 70 years, which is consistent with most of the findings [14,16,40]. However, some studies have found that age is not an influencing factor for ROSC and survival [41,42]. Larsen et al. [43] showed statistically significant data for patients aged >60 years, but not for patients age >70 years. This may be due to the fact that their study population mainly included patients between 60 and 70 years old; whereas 53.9% of patients in our study were over 70 years old. However, elderly patients are more likely to refuse CPR; therefore, the data may not fully represent the entire elderly population.

4.3. Impact of resuscitation duration on IHCA outcomes

IHCA outcomes have been associated with the duration of resuscitation. We noted that patients at hospitals in which the duration of resuscitation attempts was shorter, had a higher likelihood of ROSC and survival to discharge than those who underwent a longer resuscitation. This finding is consistent with those of multiple studies [44,45]. We compared the patients with longer resuscitation attempts versus shorter attempts, and found that 56.7% patients survived to discharge when the resuscitation time was shorter than 15 min, but only 3.1% survived when the resuscitation effort extended beyond 30 min. Goldberger et al. showed that in order for patients to achieve ROSC, the medium duration of resuscitation was 12 min (IQR 6–21) compared with 20 min (14–30) for non-ROSC [24]. However, the duration of resuscitation is often influenced by the family caregiver. Some families do not want to give up on resuscitation, due to the tenets of the Chinese culture, which leads to an indefinite extension of recovery time, even >1–2 h. During our study period, the Hospice Palliative Care Act had not been implemented at our study hospitals; physicians could not withhold CPR from patients, even those who would not derive a benefit from it. Therefore, we included a number of unnecessary CPR events in our findings. The optimal duration for resuscitation has always been a challenge for medical staff.

4.4. Impact of comorbidity on IHCA outcomes

Based on our study findings, comorbidity was an independent factor for survival to discharge. The survival rate of CCI ≤2 points was 6.71 times when compared with CCI >2 points. CCI was initially used to predict mortality one year after discharge [32]; Piscator et al. [46] assessed the impact of the age-combined Charlson Co-morbidity Index (ACCI) on 30-day survival after IHCA. They found that with increased ACCI scores, the 30-day survival rate decreased; the OR of the 5 to 7 points group and ≥8 points groups were 0.10 and 0.04, respectively, when compared with those of the 0 to 4 points group. However, Winthe et al. and Terman et al. found that comorbidity did not independently predict the prognosis of cardiac arrest [47,48], which is inconsistent with our study. The main reason, is that their studies did not stratify ACS patients. The health of ACS patients is often complicated by such conditions as cardiac insufficiency, and liver or kidney dysfunction; all of which may affect

Table 2
Univariate regression analysis for ROSC and survival to discharge

Factors		N (%)	ROSC			Survival to discharge		
			N (%)	*P*	*OR* (95%CI)	N (%)	*P*	*OR* (95%CI)
Age, years	≥70	182 (56.9)	56 (30.8)		1.000	16 (8.8)		1.000
	<70	138 (43.1)	78 (56.5)	<0.001	2.93 (1.8–4.64)	52 (37.5)	<0.001	6.27 (3.38–11.64)
Location								
ICU		194 (60.6)	72 (37.1)		1.000	33 (17.0)		1.000
General ward		87 (27.2)	52 (59.8)	0.619	1.14 (0.68–1.92)	15 (17.2)	0.962	1.02 (0.52–1.99)
Catheterization room		33 (10.3)	10 (30.3)	<0.001	3.90 (1.76–8.65)	18 (54.5)	<0.001	5.86 (2.68–12.78)
Others		6 (1.9)	4 (66.7)	0.165	3.39 (0.61–18.97)	2 (33.3)	0.315	2.44 (0.43–13.87)
Initial rhythm								
Shockable rhythm		140 (43.8)	87 (62.1)	<0.001	4.65 (2.88–7.48)	53 (37.9)	<0.001	6.70 (3.57–12.57)
Non-shockable rhythm		180 (56.3)	47 (26.1)		1.000	15 (8.3)		
Duration of resuscitation, min					32.50 (10.75–55.25)			
≤15		97 (30.9)	90 (92.8)		1.000	55 (56.7)	<0.001	41.12 (15.48–109.21)
16–30		55 (17.5)	20 (36.4)	<0.001	77.70 (32.02–188.58)	7 (12.7)	0.012	4.58 (1.39–15.09)
>30		162 (51.6)	23 (14.2)	0.001	3.45 (1.71–6.99)	5 (3.1)		1.000
Resuscitation attempt								
A		84 (26.3)	18 (21.4)		1.000	11 (13.1)		1.000
B		112 (35.0)	77 (68.8)	<0.001	8.07 (4.18–15.56)	50 (44.6)	<0.001	5.35 (2.57–11.16)
C		66 (20.6)	20 (30.3)	0.217	1.59 (0.76–3.34)	1 (1.5)	0.031	0.10 (0.27–2.20)
D		58 (18.1)	19 (32.8)	0.133	1.79 (0.84–3.81)	6 (10.3)	0.620	0.77 (0.27–2.20)
CCI ≤2		175 (54.7)	77 (44.0)	0.397	1.21 (0.78–1.90)	52 (29.7)	<0.001	3.41 (1.85–6.29)
Prior PCI		90 (28.5)	51 (56.7)	0.001	2.34 (1.42–3.58)	32 (35.6)	<0.001	3.01 (1.72–5.28)
Smoking		113 (35.3)	51 (45.1)	0.001	2.28 (1.43–3.60)	33 (29.2)	0.011	2.03 (1.18–3.49)
Killip ≤II		98 (30.6)	46 (46.9)	0.223	1.35 (0.83–2.18)	38 (38.8)	<0.001	4.05 (2.32–7.09)
Length of hospital stay prior to IHCA, days								
≤1		138 (43.3)	35 (25.4)	0.105	1.47 (0.87–2.50)	62 (44.9)	0.006	2.78 (1.33–5.79)
2–5		80 (25.1)	21 (26.3)	0.268	1.40 (0.77–2.56)	35 (43.8)	0.009	2.91 (1.31–6.48)
≥6		101 (31.7)	11 (10.9)		1.000	36 (35.6)		1.000

the outcome. In addition, Terman et al. limited their study to older adults, but our study included all adult patients.

5. Limitations

There are also some limitations in our study. First, it is a retrospective observational cohort study; there are confounding factors that might affect our results, for instance, there may also be inaccuracies and missing data in documentation, since there is no established multicenter database in Fujian to collect cardiac arrest data prospectively.

Second, the database only recorded in-hospital deaths. Many patients discharged "against medical advice" preferred to die at home instead of in hospital, due to the tenets of traditional Chinese culture. This would be classified as in-hospital death according to our study; hence the incidence of survival to discharge may be underestimated.

Finally, we investigated only three hospitals in one region; all three are level III hospitals; hence, there may be some bias in population choice. And the sample size was insufficient to analyze variations across hospitals or across specific patient subgroups. Further studies should include more hospitals, including Level I and II hospitals, as a requirement.

6. Conclusion

Based on data from multiple centers in China, the in-hospital cardiac arrest outcomes of ACS patients are slightly better than the outcomes of overall inpatients that had previously been reported. Younger age, shockable rhythm, and a shorter duration of resuscitation were all demonstrated to be predictors of ROSC and survival to hospital discharge. Prior PCI was associated with ROSC but not survival to discharge, however, the Killip classification was associated with survival.

Ethics approval and consent to participate

The Ethics Committee Board of Fujian Provincial Hospital approved this study and waived the requirement for written informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare they have no competing interests.

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None.

Table 3
Multivariate logistic regression analysis for ROSC

Variables		*β*	*S.E*	*Wald* χ^2	*P*	*OR*	*95%CI*
Age <70 years-old		1.58	0.41	14.67	<0.001	4.87	2.17–10.95
Shockable rhythm		1.48	0.42	12.31	<0.001	4.40	1.92–10.06
Duration of resuscitation	≤15 min	3.47	0.55	40.03	<0.001	32.05	10.95–93.83
	16–30 min	1.67	0.67	6.20	0.013	5.34	1.92–10.06
Prior PCI		0.88	0.41	4.61	0.032	2.40	1.08–5.35

Table 4
Multivariate logistic regression analysis for survival to discharge

Variables		*β*	*S.E*	*Wald* χ^2	*P*	*OR*	*95%CI*
Age <70 years-old		1.41	0.46	9.53	0.002	4.10	1.67–10.02
Shockable rhythm		1.97	0.51	15.20	<0.001	7.19	2.67–19.37
Duration of resuscitation	≤15 min	4.29	0.69	38.51	<0.001	73.02	18.83–283.13
	16–30 min	1.79	0.76	5.58	0.018	6.01	1.36–26.61
Killip ≤II		1.73	0.52	10.96	0.001	5.63	2.02–15.66
CCI ≤2		1.90	0.55	12.03	0.001	6.71	2.29–19.68

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